

## MASS SPECTROMETRY PROBES AND SYSTEMS FOR IONIZING A SAMPLE

### RELATED APPLICATIONS

[0001] The present application is a continuation of U.S. nonprovisional application Ser. No. 16/516,823, filed Jul. 19, 2019, which is a continuation of U.S. nonprovisional application Ser. No. 15/104,405, filed Jun. 14, 2016, which is a 35 U.S.C. § 371 national phase application of PCT/US14/71856, filed Dec. 22, 2014, which claims the benefit of and priority to each of U.S. provisional patent application Ser. No. 61/926,713, filed Jan. 13, 2014, and Indian patent application number 6137/CHE/2013, filed Dec. 30, 2013, the content of each of which is incorporated by reference herein in its entirety.

### GOVERNMENT SUPPORT

[0002] This invention was made with government support under CHE1307264 awarded by the National Science Foundation. The government has certain rights in the invention.

### FIELD OF THE INVENTION

[0003] The invention generally relates to mass spectrometry probes and systems for ionizing a sample.

### BACKGROUND

[0004] Recent progress in mass spectrometry has depended heavily on advances in methods of ion formation. Creation of stable molecular ions of complex molecules with minimum internal energy has been a primary goal of such experiments. The most widely used methods to achieve this are electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI). The newer ambient ionization methods, such as desorption electrospray ionization (DESI), allow samples to be examined in their native state with minimal or no sample pre-treatment. These advantages and the resulting speed of analysis have led to the introduction of some fifty different variants of ambient ionization. Direct analysis in real time (DART), extractive electrospray ionization (EESI), desorption atmospheric pressure chemical ionization (DAPCI), desorption atmospheric pressure photoionization (DAPPI), laser ablation electrospray ionization (LAESI), and paper spray ionization, are some of the new methods introduced over the past decade.

[0005] Many of those methods use a high voltage source coupled to the probe to achieve ionization in an ambient environment. The application of high voltage can sometimes cause unwanted fragmentation of a target analyte during the ionization process.

### SUMMARY

[0006] The invention provides a low voltage mass spectrometry probe configured to generate ions without the need for a high voltage source. Aspects of the invention are accomplished with a substrate in which a portion of the substrate is coated with a material, a portion of which protrudes from the substrate. Generally, these protrusions are on the nanoscale and, without being limited by any particular theory or mechanism of action, act as an electrode. The protrusions provide a field strength high enough to cause field emission of microscale solution droplets containing analyte at these nanoscale protrusions. In that man-

ner, mass spectrometry probes of the invention are able to ionize a target analyte through the application of a low voltage (e.g., 3 volts or less), rather than a high voltage, allowing for ionization without unwanted fragmentation of the target analyte.

[0007] In certain aspects, the invention provides a mass spectrometry probe including a substrate. The substrate can be porous or nonporous. An exemplary substrate is a paper substrate, such as a substrate composed of filter paper. The substrate can have any shape. In certain embodiments, the substrate tapers to a tip, such as a substrate including a planar portion that tapers to a tip. An exemplary shape is a triangular substrate that tapers to a tip.

[0008] The probe further includes a material that coats a portion of the substrate. A portion of that material protrudes from the substrate. In certain embodiments, the material is an electrically conductive material, although that is not required, because a solvent surrounding the material can be an electrolyte in some cases. Any electrically conductive material may be used with probes of the invention. An exemplary material includes electrically conductive nanotubes, such as carbon nanotubes. Typically, the carbon nanotubes coat an external surface of the substrate, and a distal portion of a plurality of the carbon nanotubes protrude from the surface of the substrate. It is also possible for portions of the carbon nanotubes, or any chosen material, to impregnate the substrate.

[0009] In certain embodiments, the substrate is coupled to a voltage source. In certain embodiments, the voltage source is configured to generate a voltage of 3 volts or less, such as 2.9 volts or less, 2.8 volts or less, 2.7 volts or less, 2.6 volts or less, 2.5 volts or less, 2.4, volts or less, 2.3 volts or less, 2.2, volts or less, 2.1 volts or less 2 volts or less, 1.5 volts or less, or 1 volt or less.

[0010] Another aspect of the invention provides a system including a mass spectrometry probe having a substrate in which a portion of the substrate is coated with a material, a portion of which protrudes from the substrate. A voltage source is coupled to the substrate, and a mass analyzer is operably associated with the system such that it receives ions generated from the mass spectrometry probe. In certain embodiments, the probe is discrete from a flow of solvent. In certain embodiments, the probe operates without pneumatic assistance. The mass analyzer can be for a bench-top mass spectrometer or a miniature mass spectrometer.

[0011] Another aspect of the invention provides a system including a mass spectrometry probe having carbon nanotubes, a voltage source coupled to the probe, and a mass analyzer. In certain embodiments, the carbon nanotubes alone make-up the probe. In other embodiments, the probe further includes a substrate (porous or non-porous) and the carbon nanotubes are coupled to the substrate.

### BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. 1A is a schematic diagram of ionization from carbon nanotube (CNT) paper. FIG. 1B is a photograph of the ionization source showing a paper triangle and battery along with a grounding electrical connection. FIG. 1C is a mass spectra of triphenylphosphine (M) at 3 kV, 3 V and 1 V from wet CNT paper. FIG. 1D is a field emission-scanning electron microscopy (FE-SEM) image of CNT-coated paper. FIG. 1E is an isotope distribution of the protonated molecule at 3 V. FIG. 1F is a product ion MS<sup>2</sup> of m/z 263.